IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Xu et al.
Prior Application No.: 09/205,995
Prior Application Filing Date: December 4, 1998
Title: MHC CLASS II ANTIGEN PRESENTING CELLS CONTAINING OLIGONUCLEOTIDES WHICH INHIBIT Ii PROTEIN EXPRESSION
Prior Application Art Unit: 1655
Prior Application Examiner: Arthur, L.

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PRELIMINARY AMENDMENT

Box PATENT APPLICATION
Commissioner for Patents
Washington, DC 20231

Dear Sir:

Preliminarily, please amend the subject patent application as described below.

In the Claims:

Cancel Claims 1-96 and add the following new claims, 97-155.

97. A method for displaying an autodeterminant peptide, in association with a MHC class II protein, on the surface of a MHC class II-positive antigen presenting cell, comprising:
a) providing the MHC class II-positive antigen presenting cell which does not contain an exogenous construct encoding mammalian B7 molecule; and
b) introducing into the MHC class II-positive antigen presenting cell, a specific regulator of Ii protein expression or immunoregulatory function, the oligonucleotide CTCGGTACCTACTGG (SEQ ID NO: 1) being specifically excluded, the specific regulator consisting essentially of a copolymer of from 10 to 50 nucleotide bases, the copolymer being characterized by the ability to hybridize specifically to a target region of the RNA molecule encoding mammalian Ii protein under physiological conditions, wherein the specific regulator is characterized by the ability to inhibit Ii expression.

98. The method of Claim 97 wherein the specific regulator of Ii is introduced into the MHC class II-positive antigen presenting cell via electroporation.

99. The method of Claim 97 wherein the target region comprises the translation initiation site of the RNA molecule encoding mammalian Ii protein.

100. The method of Claim 99 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 54, 53, 52, 40 and 55.

101. The method of Claim 97 wherein the target region comprises a portion of an exon bounding a splice site.

102. The method of Claim 101 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 32 and 62.

103. The method of Claim 97 wherein the target region is within an exon/intron boundary.

104. The method of Claim 103 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 64 and 48.

105. A therapeutic method for treating a malignancy in a patient by enhancing immunological attack on the malignancy, comprising:

a) providing a population of malignant cells and, if necessary, inducing expression of MHC class II molecules, the cells comprising the population of malignant cells lacking an exogenous construct encoding mammalian B7 molecule;

b) introducing into the MHC class II-expressing malignant cells of step a), a specific regulator of Ii protein expression to enhance presentation of endogenous antigenic determinants, the oligonucleotide CTCGGTACCTACTGG (SEQ ID NO: 1) being specifically excluded, the specific regulator consisting essentially of a copolymer of from 10 to 50 nucleotide bases, the copolymer being characterized by the ability to hybridize specifically to a target region of the RNA molecule encoding mammalian Ii protein under physiological conditions, wherein the specific regulator is characterized by the ability to inhibit Ii expression; and

c) introducing the cells produced by step b) into the patient.

106. The therapeutic method of Claim 105 wherein the cells produced by step b) are made replication incompetent prior to step c).

107. The therapeutic method of Claim 105 wherein the specific regulator of Ii protein expression is introduced into the MHC class II-expressing malignant cells via electroporation.

108. The therapeutic method of Claim 105 wherein the population of malignant cells of step a) is obtained from the patient.

109. The method of Claim 105 wherein the target region comprises the translation initiation site of the RNA molecule encoding mammalian Ii protein.

110. The method of Claim 109 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 54, 53, 52, 40 and 55.

111. The method of Claim 105 wherein the target region comprises a portion of an exon bounding a splice site.

112. The method of Claim 111 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 32 and 62.

113. The method of Claim 105 wherein the target region is within an exon/intron boundary.

114. The method of Claim 113 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 64 and 48.

115. A therapeutic method for treating a malignancy in a patient by enhancing immunological attack on the malignancy, comprising:

a) providing a population of cells either expressing or containing antigenic determinants of the malignancy and, if necessary, inducing expression of MHC class II molecules, the cells comprising the population of malignant cells lacking an exogenous construct encoding mammalian B7 molecule;

b) introducing into the MHC class II-expressing cells of step a) a specific regulator of Ii protein expression to enhance presentation of endogenous antigenic determinants, the oligonucleotide CTCGGTACCTACTGG (SEQ ID NO: 1) being specifically excluded, the specific regulator consisting essentially of a copolymer of from 10 to 50 nucleotide bases, the copolymer being characterized by the ability to hybridize specifically to a target region of the RNA molecule encoding mammalian Ii protein under physiological conditions, wherein the specific regulator is characterized by the ability to inhibit Ii expression; and

c) introducing the cells produced by step b) or a derivative thereof, into the patient.

116. The therapeutic method of Claim 115 wherein the cells produced by step b) are made replication incompetent prior to step c).

117. The therapeutic method of Claim 115 wherein the specific regulator of Ii protein expression is introduced into the MHC class II-expressing cells via electroporation.

118. The therapeutic method of Claim 115 wherein the population of cells of step a) is obtained from the patient.

119. The method of Claim 115 wherein the target region comprises the translation initiation site of the RNA molecule encoding mammalian Ii protein.

120. The method of Claim 119 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 54, 53, 52, 40 and 55.

121. The method of Claim 115 wherein the target region comprises a portion of an exon bounding a splice site.

122. The method of Claim 121 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 32 and 62.

123. The method of Claim 115 wherein the target region is within an exon/intron boundary.

124. The method of Claim 123 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 64 and 48.

125. A therapeutic method for treating a malignancy in a patient comprising administering to the patient a specific regulator of Ii protein expression or immunoregulatory function in an amount sufficient to induce an anti-cancer immune response, the oligonucleotide CTCGGTACCTACTGG (SEQ ID NO: 1) being specifically excluded, the specific regulator consisting essentially of a copolymer of from 10 to 50 nucleotide bases, the copolymer being characterized by the ability to hybridize specifically to a target region of the RNA molecule encoding mammalian Ii protein under physiological conditions, wherein the specific regulator is characterized by the ability to inhibit Ii expression.

126. The therapeutic method of Claim 125 wherein the administered amount is between 10 μg and 100 mg daily.

127. The therapeutic method of Claim 125 wherein the mode of administration is selected from the group consisting of intravenous infusion, infusion into a body cavity, absorption across skin, absorption across a mucosal surface, and absorption across the gastrointestinal tract.

128. The therapeutic method of Claim 125 wherein the specific regulator of Ii protein expression or immunoregulatory function is administered with a pharmaceutically acceptable carrier.

129. The method of Claim 125 wherein the target region comprises the translation initiation site of the RNA molecule encoding mammalian Ii protein.

130. The method of Claim 129 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 54, 53, 52, 40 and 55.

131. The method of Claim 125 wherein the target region comprises a portion of an exon bounding a splice site.

132. The method of Claim 131 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 32 and 62.

133. The method of Claim 125 wherein the target region is within an exon/intron boundary.

134. The method of Claim 133 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 64 and 48.

135. A therapeutic method for treating a nonmalignant condition in an individual by enhancing immunological attack on an undesired cell population of the individual, the method comprising:

a) providing cells from the undesired cell population and, if necessary, inducing expression of MHC class II molecules, the cells comprising the population of malignant cells lacking an exogenous construct encoding mammalian B7 molecule;

b) introducing into the MHC class II-expressing cells of step a) a specific regulator of Ii protein expression to enhance MHC CLASS II presentation of antigenic determinants, the oligonucleotide CTCGGTACCTACTGG (SEQ ID NO: 1) being specifically excluded, the specific regulator consisting essentially of a copolymer of from 10 to 50 nucleotide bases, the copolymer being characterized by the ability to hybridize specifically to a target region of the RNA molecule encoding mammalian Ii protein under physiological conditions, wherein the specific regulator is characterized by the ability to inhibit Ii expression; and

c) re-introducing the cells produced by step b) into the individual.

136. The therapeutic method of Claim 135 wherein the cells produced by step b) are made replication incompetent prior to step c).

137. The therapeutic method of Claim 135 wherein the specific regulator of Ii protein expression is introduced into the MHC class II-expressing cells via electroporation.

138. The therapeutic method of Claim 135 wherein the undesired cell population comprises autoreactive T lymphocytes which are associated with an autoimmune disorder.

139. The therapeutic method of Claim 135 wherein the undesired cell population comprises virus-infected cells.

140. The therapeutic method of Claim 135 wherein the target region comprises the translation initiation site of the RNA molecule encoding mammalian Ii protein.

141. The therapeutic method of Claim 140 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 54, 53, 52, 40 and 55.

142. The method of Claim 135 wherein the target region comprises a portion of an exon bounding a splice site.

143. The method of Claim 142 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 32 and 62.

144. The method of Claim 135 wherein the target region is within an exon/intron boundary.

145. The method of Claim 144 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 64 and 48.

146. A therapeutic method for treating an autoimmune disease in a patient comprising administering to the patient a specific regulator of Ii protein expression or immunoregulatory function in an amount sufficient to induce an anti-disease immune response, the oligonucleotide CTCGGTACCTACTGG (SEQ ID NO: 1) being specifically excluded, the specific regulator consisting essentially of a copolymer of from 10 to 50 nucleotide bases, the copolymer being characterized by the ability to hybridize specifically to a target region of the RNA molecule encoding mammalian Ii protein under

physiological conditions, wherein the specific regulator is characterized by the ability to inhibit Ii expression.

147. The therapeutic method of Claim 146 wherein the administered amount is between 10 μg and 100 mg daily.

148. The therapeutic method of Claim 146 wherein the mode of administration is selected from the group consisting of intravenous infusion, infusion into a body cavity, absorption across skin, absorption across a mucosal surface, and absorption across the gastrointestinal tract.

149. The therapeutic method of Claim 146 wherein the specific regulator of Ii protein expression or immunoregulatory function is administered with a pharmaceutically acceptable carrier.

150. The method of Claim 146 wherein the target region comprises the translation initiation site of the RNA molecule encoding mammalian Ii protein.

151. The method of Claim 150 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 54, 53, 52, 40 and 55.

152. The method of Claim 146 wherein the target region comprises a portion of an exon bounding a splice site.

153. The method of Claim 152 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 32 and 62.

154. The method of Claim 153 wherein the target region is within an exon/intron boundary.

155. The method of Claim 154 wherein the specific regulator comprises a nucleotide base sequence selected from the group consisting of SEQ ID NOS: 64 and 48.

In the Specification:

Please delete the existing title of the application, "CANCER CELL VACCINE", and substitute therefor the following new title, ---MHC CLASS II ANTIGEN PRESENTING CELLS CONTAINING OLIGONUCLEOTIDES WHICH INHIBIT Ii PROTEIN EXPRESSION---.

Please insert, before the Background of the Invention, the following paragraph:

Related Applications

This application is a division of U.S. Application No. 09/205,995 (pending), which is a continuation-in-part of U.S. Application No. 09/036,746 (now abandoned), which is a continuation of U.S. Application No. 08/661,627 (now U.S. Patent No. 5,726,020).

On page 7, line 11, after "CTCGGTACCTACTGG", insert --(SEQ ID NO: 1)--.

On page 48, row 18, second column, under "(5'- ATC CAT GGC TCT AGC CTC)*", insert --(SEQ ID NO: 2)--.

On page 48, row 19, second column, under "(5'- TCT AGC CTC TAG TTT TTC)*", insert --(SEQ ID NO: 3)--.

On page 49, line 7, after "and 44 (without deletion)", delete "was" and insert --are-- therewith.

On page 49, line 7, after "shown in bracket", please add an "s" onto "bracket, delete "was", and insert --were-- therewith.

On page 49, line 9, please add an "s" to "experiment" and delete "shown in Table 4".

On page 63, line 7, after "modification of the same sequence", insert --(SEQ ID NO: 54)--.

On page 63, line 8, delete "SEQ ID NO", and insert --(OLIGO)-- therewith.

On page 63, line 10, delete "SEQ ID NO", and insert --(OLIGO)-- therewith.

On page 63, line 13, delete "SEQ ID NO", and insert --(OLIGO)-- therewith.

On page 63, line 14, delete "SEQ ID NO", and insert --(OLIGO)-- therewith.

On page 63, line 20, delete "SEQ ID NO:" after "Oligonucleotide".

On page 63, line 20, after "54 and", delete "SEQ ID NO:", and insert --oligonucleotide-- therewith.

On page 64, Table 7, column 1 heading, please delete "SEQ ID" and insert --OLIGO-- therewith.

On page 64, Table 7, second row of column 1, under "54", insert --(SEQ ID NO: 54)--.

On page 64, Table 7, third row of column 1, under "65", insert --(SEQ ID NO: 54)--.

On page 64, Table 7, fourth row of column 1, under "67", insert --(SEQ ID NO: 54)--.

On page 65, table 8, delete "SEQ ID" from the left column heading.

Please insert the attached Sequence Listing after page 77, and renumber the Claims pages to begin with page 100.

Sequence Listing

Applicants have provided the attached paper copy of the Sequence Listing prepared in accordance with the provisions of 37 CFR 1.825. Instruction for amendment of the Specification to incorporate reference to appropriate SEQ ID NOS. and also the Sequence Listing is provided above. Applicant's Attorney hereby states that the above amendments to the Specification and Claims include no new matter.

Also transmitted herewith is a copy of the Sequence Listing in computer readable form. As required by 37 CFR 1.821 (e) or

1.821 (f) or 1.821 (g) or 1.825 (c) or 1.825 (d), Applicant's Attorney hereby states that the content of the Sequence Listing in paper form and computer readable form are the same and include no new matter.

REMARKS

In light of the above amendment, consideration of the subject patent application is respectfully requested. Please charge any deficiency or overpayment to Deposit Account No. 06-0130.

Respectfully submitted,

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